Claims

1. A method for the treatment of a subject in need of treatment for osteoarthritis comprising administering to said subject an amount of an inhibitor of spermidine biosynthesis sufficient to effect a substantial inhibition of spermidine biosynthesis so as to thereby treat the subject.

2. The method according to claim 1, wherein said inhibitor is a spermidine synthase inhibitor.

3. The method of claim 2 wherein said spermidine synthase inhibitor is selected from the group consisting of adenosyl spermidine, AdoDATO, DCHA, trans-4-methylcyclohexylamine (4MCHA), cyclohexylamine, methylglyoxal bis (cyclopentylamidinohydrazone) (MGBP), 2-mercaptopropylamine, N-chlorosulfonyldicyclohexylamine, 5'-((3-aminopropyl) amino)-5'-deoxyadenosine, 1-aminooxyl-3-aminopropane, 5'-(isobutylthio) adenosine, 5'-(methylthio) adenosine and any functional homologs and analogs thereof.

4. Use of an inhibitor of spermidine biosynthesis in the treatment of a subject in need of treatment for osteoarthritis in an amount sufficient to effect a substantial inhibition of spermidine biosynthesis so as to thereby treat the subject.

5. The use according to claim 4, wherein said inhibitor of spermidine biosynthesis is a spermidine synthase inhibitor.

6. The use according to claim 5, wherein said inhibitor is selected from the group consisting of adenosyl spermidine, AdoDATO, DCHA, trans-4-

methylcyclohexylamine (4MCHA), cyclohexylamine, methylglyoxal bis-(cyclopentylamidinohydrazone) (MGBP), 2-mercaptopropylamine, N-chlorosulfonyldicyclohexylamine, 5'-((3-aminopropyl)amino)-5'-deoxyadenosine, 1-aminooxyl-3-aminopropane, 5'-(isobutylthio) adenosine, 5'-(methylthio) adenosine and any functional homologs and analogs thereof.

7. Use of an inhibitor of spermidine biosynthesis in the preparation of a pharmaceutical composition for the treatment of a subject in need of treatment for osteoarthritis.

8. The use according to claim 7, wherein said inhibitor of spermidine biosynthesis is a spermidine synthase inhibitor.

9. The use according to claim 8, wherein said inhibitor is selected from the group consisting of adenosyl spermidine, AdoDATO, DCHA, trans-4-methylcyclohexilamine (4MCHA), cyclohexylamine, methylglyoxal bis-(cyclopentylamidinohydrazone) (MGBP), 2-mercaptopropylamine, N-chlorosulfonyldicyclohexylamine, 5'-((3-aminopropyl)amino)-5'-deoxyadenosine, 1-aminooxyl-3-aminopropane, 5'-(isobutylthio) adenosine and 5'-(methylthio) adenosine and any functional homologs and analogs thereof.

10. A therapeutic composition for the treatment of a subject in need of treatment for osteoarthritis comprising an amount of an inhibitor of spermidine biosynthesis sufficient to effect a substantial inhibition of spermidine biosynthesis, and a carrier.

11. The therapeutic composition according to claim 10, wherein said inhibitor of spermidine biosynthesis is a spermidine synthase inhibitor.

12. The therapeutic composition according to any one of claims 10 and 11, wherein said carrier is a pharmaceutically or veterinarily acceptable carrier.

13. A method of preparing a therapeutic composition for the treatment of a subject in need of a treatment for osteoarthritis, which method comprises the steps of:
    a. obtaining an amount of an inhibitor of spermidine biosynthesis sufficient to effect a substantial inhibition of spermidine biosynthesis, and
    b. admixing said inhibitor with a pharmaceutically acceptable carrier.

14. A method of identifying an inhibitor of spermidine biosynthesis, whereby the inhibitor is a spermidine synthase inhibitor and whereby the identification is performed by the steps of:
    a. obtaining a candidate spermidine synthase inhibitor;
    b. evaluating the effect of said candidate inhibitor as compared to a control on any one of chondrocyte proliferation, chondrocyte final differentiation, angiogenesis and osteoclastogenesis by an evaluating method

15. The method of claim 14 wherein the evaluating method comprises the steps of:
    i. providing a test system comprising DNA encoding spermidine synthase;

ii. contacting said system with the said test candidate spermidine synthase inhibitor under conditions which normally lead to expression of spermidine; and

iii. determining the effect of the test candidate inhibitor on an end-point indication as compared to a control, wherein said effect is indicative of inhibition of any one of chondrocyte proliferation, chondrocyte final differentiation, angiogenesis and osteoclastogenesis by the test candidate inhibitor..

16. The method according to claim 15, wherein said test system is an *in vitro* transfected cell culture comprising an exogenously expressed spermidine synthase.

17. The method according to claim 16, wherein said transfected cell culture is a culture of RCJ3.1C5.18 cells stably transfected with pCMVneo expression vector comprising a nucleic acid sequence coding for the spermidine synthase protein.

18. The method according to claim 15, wherein said test system is an *ex vivo* bone culture comprising an endogenously expressed spermidine synthase.

19. The method according to claim 18, wherein said bone culture is an embryonic bone culture.

20. The method according to claim 15, wherein said test system is an *in vivo* test system comprising an animal model.

21. The method according to claim 20, wherein said end point indication is development of arthritis.

22. The method according to claim 21, wherein the development of arthritis is determined by paw thickness of said animal, wherein less increase of the size of the paw as compared to a control is indicative of inhibition of any one of chondrocyte proliferation, chondrocyte final differentiation, angiogenesis and osteoclastogenesis and development of arthritis by said test candidate inhibitor.

23. The method according to any one of claims 20 to 22, wherein said animal model is a transgenic mouse.

24. The method according to claim 20, wherein said *in vivo* test system is an arthritic mammalian model expressing endogenous spermidine synthase.

25. The method according to claim 24, wherein said end point indication is development of arthritis.

26. The method according to claim 25, wherein the development of arthritis is determined by paw thickness of said arthritic mammal, wherein less increase of the size of the paw as compared to a control is indicative of inhibition of any one of chondrocyte proliferation, chondrocyte final differentiation, angiogenesis and osteoclastogenesis, and development of arthritis by said test candidate inhibitor.

27. The method according to any one of claims 24 to 26, wherein said arthritic mammal is an arthritic rat.

28. The method according to claim 14, wherein obtaining a candidate spermidine synthase inhibitor is by selecting an inhibitor from the group

consisting of adenosyl spermidine, AdoDATO, DCHA, trans-4-methylcyclohexylamine (4MCHA), cyclohexylamine, methylglyoxal bis (cyclopentylamidinohydrazone) (MGBP), 2- mercaptopropylamine, N-chlorosulfonyldicyclohexylamine, 5'-((3-aminopropyl) amino)-5'-deoxyadenosine, 1-aminooxyl-3-aminopropane, 5'-(isobutylthio) adenosine, 5'-(methylthio) adenosine and any functional homologs and analogs thereof.

29. The method according to claim 14, wherein obtaining a candidate spermidine synthase inhibitor is performed by a screening method for a substance which is an inhibitor of spermidine synthase, which screening method comprises the steps of:

a. providing a mixture comprising spermidine synthase;

b. contacting said mixture with a test substance under conditions which normally lead to biosynthesis of spermidine; and

c. determining the effect of the test substance on an end-point indication, whereby inhibition of said end point is indicative of inhibition of spermidine synthase by the test substance.

30. The method according to claim 29, wherein the end point indication is the presence of a product of spermidine synthase catalytic reaction.

31. The method according to claim 30, wherein the presence of a product of spermidine synthase catalytic reaction leads to any one of fluorescent or radioactive detectable signals.